UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,935	02/15/2006	Kappei Tsukahara	082368-004400US	6397

20350 7590 05/27/2010

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
05/27/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,935	TSUKAHARA ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/8/2010 and 3/10/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed 2-8-10 and 3-9-10. Claims 1-6 and 9-10 are pending and under examination. Claims 2 and 4 have been amended.

Objections/Rejections Withdrawn

2. In view of the Applicant's amendments and remarks the following objections/rejections are withdrawn.

a) Objection to the specification because of the phrases "GlcN-(acyl)PI", "GPI", and "GPI-anchored" (see pgs. 1-2); objection to specification because it contained an embedded hyperlink and/or other form of browser-executable code (see pg. 3 lines 25-30), and objection to the specification because of the use of the trademarks (see pg. 9 lines 10-20) are withdrawn in light of applicant's amendment to the specification filed 2/8/2010.

b) Objection to claim 1-6 and 9-10 because of the claims contained abbreviations "GlcN-(acyl)PI", "GPI", and "GPI-anchored" is withdrawn in light of applicant's amendment thereto.

c) Rejection of claims 1-2 and 9-10 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7,541,332 is withdrawn in light of applicant's arguments.

d) Rejection of claims 1-6 and 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Sequence Requirements

3. This application contains a sequence disclosure encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application is in full compliance with the requirements of 37 C.F.R. § 1.824.

Information Disclosure Statement

4. The information disclosure statements filed 2/8/2010 and 3/10/2010 have been considered. Initialed copies are enclosed.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

5. The rejection of claims 1-6 and 9-10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement are maintained for the reasons set forth in the previous office action. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicants arguments filed in response to the 35 U.S.C. 112 first, paragraph, February 8, 2010 is carefully considered, but not found to be persuasive for the reasons below.

Applicant argues:

A) As an initial matter, Applicants note that the Examiner has apparently misunderstood the function of GWT1. For example at page 6, lines 25-27 of the Office Action, the Examiners states that "[t]he specification is only limited the S. Cerevisiae GWTI gene comprising the nucleotide sequence of SEQ 1I) NO: 1 capable of decreasing GlcN-(acyl)PI" (emphasis added). In fact, as discussed above, the function of GWT1 is to catalyze the transacylation of GPI, thus forming GlcN-(acyl)PI. Activity of the enzyme therefore leads to increased levels of GlcN-(acyl)PI, not decreased levels. While not necessarily agreeing with the Examiner's assertions, the Applicants have amended claim 2 to further specify the claimed proteins. Specifically, stringent conditions have been defined in claim 2(c) and the number of amino acid residues which have been added, deleted, substituted, and/or inserted has been specified in claim 2(d). Furthermore, a DNA has been added in claim 2(e), encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14. As explained in detail below, the

DNAs of amended claim 2(c), (d) and (e) would be expected to encode proteins having the same function of the original GWT1 as set forth SEQ ID NOs: 2,4,6,8, 10, or 14 as explained below.

B) Applicants provide herewith two references published after filing date of the present application. The first reference, Umemura, et al (J. Biol. Chem. 278:23639-23647 (2003), Appendix A) teaches that GWT1 of Schizosaccharomyces pombe and Cryptococcus neoformans catalyze the transacylation of GPI (see page 23664, lines 16-23 of right column). In addition, pair-wise alignments between the amino acid sequences of GWT1 of Saccharomyces cerevisiae ("EI-A0209P-2", SEQ ID NO: 2), Schizosaccharomycespombe ("EI-A0209P-8", SEQ ID NO: 8) and Cryptococcus neoformans ("E1-A0209P-14", SEQ ID NO: 14) are shown in the attached Appendix B. These alignments show that the identity between these three amino acid sequences is at least about 30%. Thus, one of skill would recognize that a protein comprising an amino acid sequence having as little as about 30% identity to one of these three amino acid sequences would also catalyze the transacylation of GPI.

C) The second reference, Murakami, et al (Mol. Biol. Cell 14:4285-4295 (2003), Appendix C) teaches that a rat enzyme identified as PIG-W (GWT1) catalyzes the transacylation of GPI (see "PIG- WIs Most Likely the Acyltransferase" at page 4289, right column). In addition, alignment results between the amino acid sequences of GWT 1 of Saccharomyces cerevisiae and rat PIG- W (Genbank accession no. BAC77020) are shown in the attached Appendix D. The results indicate that the identity between these two amino acid sequences is also about 30%. This information provides further evidence to show that a protein comprising an amino acid sequence as little as about 30% identical to one of these two amino acid sequences catalyzes the transacylation of GPI.

D) The proteins encoded by the DNAs of amended claim 2(d) and (e) comprise a amino acid sequence having more than 60% identity to these three amino acid sequences, and thus it would be recognized that the claim is directed to proteins that catalyze the transacylation of GPI. Also, since stringent conditions have been defined in claim 2(c), DNAs encoding a protein having less than 30% identity to these three amino acid sequences would not be encompassed in the DNA of amended claim 2(c). Moreover, the specification provides clear instructions and actual examples of methods for testing transacylation of GPI (see 2. Methods for determining transacylation activity, beginning on page 6 of the present application). Thus, variants can be

readily tested for this activity. Accordingly, in view of the evidence provided here, one of skill would recognize that GWT1 variants as defined by amended claim 2 will catalyze transacylation of GPI and would thus be useful in the claimed methods.

E) The Examiner also questions whether there is a correlation between compounds identified by the claimed methods and antifungal activity. However, US 2004/0038239 (Appendix E) corresponding to US Application No. 10/332,340 discloses that compounds identified by the claimed methods (for example 1-(4-butylbenzyl) isoquinoline, which is described on pages 10-11 of the present application) have antifungal activity and inhibit the growth of Saccharomyces cerevisiae and Candida albicans. Thus, compounds identified by the claimed methods clearly correlate with the antifungal activity.

Examiners Response to Applicants Arguments:

With regard to Points (A), (B), and (D), the Examiner understands the function of GWT1 is to catalyze the transacylation of GPI, thus forming GlcN-(acyl)PI. Activity of the enzyme therefore leads to increased levels of GlcN-(acyl)PI, not decreased levels. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph. Applicants must adequately describe the genus of GWT1 gene in a test sample capable of possessing the functional limitations in screening for antifungal activity comprising method steps 1), 2), and 3). The specification discloses only the detection of acylated GPI in GWT1 gene-introduced wild-type strain isolated from *Saccharomyces Cerevisiase (S. Cerevisiase).* The specification states the compounds of Examples (B2, B60, B73, and B85) disclose the GWT1 gene. The specification discloses that acylated GPI was inhibited by compounds in example B2 and B60 (see Figure 4). Therefore the specification only contemplates GWT1 gene can be screened using acylated GPI (GlcN-(acyl)PI) as an indicator because the compounds as set forth supra inhibit GlcN-(acyl)PI. Hence, the correlation between the detection of acylated GPI in said GWT1 gene-introduced wild-type strain merely suggest that GlcN-(acyl)PI decreased in a test sample having antifungal activity will indicate inhibitory activity of GWT1 gene in an assay. Additionally, there is no correlation between structure and enzyme function. The specification is only limited the *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) comprising the nucleotide sequence of SEQ ID NO:1 capable of increasing GlcN-(acyl)PI and the detection of an acylated GPI in GWT1 gene-introduced wild-type strain isolated from *Saccharomyces Cerevisiase (S. Cerevisiase).*

Furthermore, Applicants have not shown how GlcN-(acyl)PI can be used as an indicator, when GlcN-(acyl)PI is added to a test sample with any overexpressed protein encoded by GWT1 gene resulting in GlcN-(acyl)PI decreased in the sample. In regards to Applicants response of DNA hybridization in 2(c) aforementioned above, the specification doesn't explicitly define what constitutes stringent conditions. Therefore, the disclosure fails to describe common attribute and characteristics that identify the variant polynucleotides and/or the subsequences that hybridizing to the full-length SEQ ID NO: 1 sequence, which have the biological activity. In regards Applicant response that the proteins encoded by the DNAs of amended claim 2(d) and (e) comprise a amino acid sequence having more than 60% identity to these three amino acid sequences aforementioned above, screening and characterizing the variant sequences or fragments require undue experimentation because targeting polynucleotide variants, cloning, expressing, and characterizing the nucleotide sequences encoding functional (e.g., anti-fungal) proteins still require a large quantity of experimentation. Consequently, Applicant has not shown the correlation of structure of *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) (or any fragment, complement etc.) in a test sample having antifungal activity possessing the functional limitations in screening for antifungal activity in a test sample comprising method steps 1), 2), and 3) as claimed. Furthermore, Applicant has not shown the correlation of the genus of GWT1 gene (SEQ ID NOs: 1, 3, 5, 7, 9, 11-13), with the functional limitations aforementioned above. Therefore, the performance of said method steps 1) 2) and 3) do not correlate to the outcome as claimed.

With regard to Points (B) and (C), the Umemura, et al (J. Biol. Chem. 278:23639-23647 (2003), disclose mutations (substitutions): W63R and V64A of S. Cerevisiae Gwtl gene (see Figure 5) that result in a temperature sensitive (Ts) phenotype which cause the Gwt1 loss of function (see page 23642, the left column, the 1st paragraph, the last sentence). Furthermore, the pair-wise alignments between the amino acid sequences of GWT1 of Saccharomyces cerevisiae ("EI-A0209P-2", SEQ ID NO: 2), Schizosaccharomycespombe ("EI-A0209P-8", SEQ ID NO: 8) and Cryptococcus neoformans ("E1-A0209P-14", SEQ ID NO: 14) shown in the attached Appendix B in Figure 5 only suggest that the mutations to the GWT1 gene can lead to a predictable outcome. Furthermore, the second reference, Murakami, et al (Mol. Biol. Cell 14:4285-4295 (2003), Appendix C) teaches that a rat enzyme identified as PIG-W is responsible

for inositol acylation and only suggest the GWT1 gene responsible for catalyzing the transacylation of GPI is complementary.

The general knowledge and level of skill in the art do not supplement the omitted description with respect to a massive number of variant sequences of peptide. An unduly level of skill is needed for the skilled artisan in order to make and characterize the variant polynucleotides and the subsequences thereof. It is noted that applicant(s) have listed nucleotide sequences (GWT1 genes of yeast strains, e.g., S. cerevisiae, from 8 different species (SEQ ID) NOs l, 3, 5, 7, 9, 11-13) which are known in the prior art and which has a percentage similarity to a claimed sequence. Absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effect of these changes are largely unpredictable as to which one have significant effect versus not. Therefore, the references of Umemura, et al and Murakami, et al cited by Applicants in regards to sequence similarity results are unpredictable and therefore unreliable correspondence between the claimed method. The biomolecule and the indicated similar biomolecule of known function lack support regarding written description. Screening and characterizing the variant sequences or fragments require undue experimentation because targeting polynucleotide variants, cloning, expressing, and characterizing the nucleotide sequences encoding functional (e.g., anti-fungal) proteins still require a large quantity of experimentation. Therefore, Applicant's response that one of skill would recognize a protein comprising an amino acid sequence having as little as about 30% identity to one of these three amino acid sequences is unpersuasive and would not catalyze the transacylation of GPI.

With regard to Point (D), in regards to Applicant response that the proteins encoded by the DNAs of amended claim 2(d) and (e) comprise a amino acid sequence having more than 60% identity to these three amino acid sequences, absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a

single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effect of these changes are largely unpredictable as to which one have significant effect versus not. Thus the 2(d) and 2(e) aforementioned above are not representative of the genus of GWT1 gene for the recited function in the method as claimed and would not be recognized or directed to proteins that catalyze the transacylation of GPI.

Moreover, the specification discloses proteins and protein mutants can be prepared by hybridization techniques normally have high homology to proteins consisting of the amino acid sequence (see pg. 3 lines 15-25). However, the specification doesn't explicitly define what constitutes stringent conditions. The mere fact that two nucleic acid sequences will hybridize under moderate or stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus, correlation between the structure and function of the claimed invention does not meet the written description requirements. Further, it is well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability with respect to the full-length nucleic acid is possible, however the claims also read on nucleotide subsequences or fragment. Finally, hybridization under conditions even high stringency would be expected to permit a great deal of variation between the two hybridizing sequences, making it even more unpredictable that the two sequences would share the same function. Thus, the recitation of "a DNA that hybridizes under stringent condition to a DNA ..." actually reads onto "percent identity" language. Thus, as for the recitation of percent identity, hybridization language in the absence of a testable function and limitations regarding both the hybridization conditions and the sequence length over which the hybridization takes place, does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

With regard to Point (E), There is no correlation between the compounds and the method of screening for a sample as claimed. The US 2004/0038239 (Appendix E) corresponding to US Application No. 10/332,340 disclose the compound (for example 1-(4-butylbenzyl) isoquinoline. The specification only discloses said compound having inhibitory activity in GPI acylation (see pages 10-11 of the present application). However the data stated does not represent the claimed method for screening for antifungal activity in a test sample with GWT1 gene. Moreover, in

response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the compound aforementioned above and identified by the claimed method that and inhibit the growth of Saccharomyces cerevisiae and Candida albicans) are not recited in the rejected claim(s).

As outlined previously, the claims are drawn to a method of screening for a compound having an antifungal activity, wherein the method comprises the steps of: (1) contacting a test sample with an overexpressed protein encoded by the GWT1 gene; (2) detecting glucosaminyl-acylphosphatidylinositol (GlcN-(acyl)PI); and (3) selecting the test sample that decreases GlcN-(acyl)PI (claim 1), wherein the GWT1 gene is any one of the following: (a) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; (b) a DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13; (c) a DNA hybridizing to the DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13 under stringent conditions, wherein the stringent conditions are hybridization in 4x SCC at 65°C followed by washing with 0.1x SSC at 65°C for one hour; (d) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14, wherein one or more amino acids have been added, deleted, substituted, and/or inserted; and (e) a DNA encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10 or 14 (claim 2), wherein the step of detecting acylated GPI is thin-layer chromatography (claim 3), wherein the method further comprises a step 4, determining whether the selected test sample inhibits the process of transporting a glucosylphosphatidylinositol-anchored (GPI-anchored) protein to a fungal cell wall, whether the test sample inhibits the expression of a GPI-anchored protein on a fungal cell surface, or whether the test sample inhibits the proliferation of a fungi (claims 5 and 9-10).

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph. The specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession of the claimed invention.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph. Applicants must adequately describe the genus of GWT1 gene in a test sample capable of possessing the functional limitations in screening for antifungal activity comprising method steps 1), 2), and 3). The specification discloses only the detection of acylated GPI in GWT1 gene-introduced wild-type strain isolated from *Saccharomyces Cerevisiase (S. Cerevisiase)*. The specification states the compounds of Examples (B2, B60, B73, and B85) disclose the GWT1 gene. The specification discloses that acylated GPI was inhibited by compounds in example B2 and B60 (see Figure 4). Therefore the specification only contemplates GWT1 gene can be screened using acylated GPI (GlcN-(acyl)PI) as an indicator because the compounds as set forth supra inhibit GlcN-(acyl)PI. Hence, the correlation between the detection of acylated GPI in said GWT1 gene-introduced wild-type strain merely suggest that GlcN-(acyl)PI decreased in a test sample having antifungal activity will indicate inhibitory activity of GWT1 gene in an assay (see pg. 10 lines 1-15). Additionally, there is no correlation between the method steps and the preamble of screening a test sample having antifungal activity in the method as claimed. The specification is only limited the *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) comprising the nucleotide sequence of SEQ ID NO:1 capable of increasing GlcN-(acyl)PI and the detection of an acylated GPI in GWT1 gene-introduced wild-type strain isolated from *Saccharomyces Cerevisiase (S. Cerevisiase)*. Furthermore, Applicants have not shown how GlcN-(acyl)PI can be used as an indicator, when GlcN-(acyl)PI is added to a test sample with any overexpressed protein encoded by GWT1 gene resulting in GlcN-(acyl)PI decreased in the sample. In regards to Applicants response of DNA hybridization in 2(c) aforementioned above, the specification doesn't explicitly define what constitutes stringent conditions. Therefore, the disclosure fails to describe common attribute and characteristics that identify the variant polynucleotides and/or the subsequences that hybridizing to the full-length SEQ ID NO: 1 sequence, which have the biological activity. In regards Applicant response that the proteins encoded by the DNAs of amended claim 2(d) and (e) comprise a amino acid sequence having more than 60% identity to these three amino acid sequences aforementioned above, screening and characterizing the variant sequences or fragments require undue experimentation because targeting polynucleotide variants, cloning, expressing, and characterizing the nucleotide sequences encoding functional (e.g., anti-fungal) proteins still require a large quantity of

experimentation. Consequently, Applicant has not shown the correlation of structure of *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) (or any fragment, complement etc.) in a test sample having antifungal activity possessing the functional limitations in screening for antifungal activity in a test sample comprising method steps 1), 2), and 3) as claimed. Furthermore, Applicant has not shown the correlation of the genus of GWT1 gene (SEQ ID NOs: 1, 3, 5, 7, 9, 11-13), with the functional limitations aforementioned above.

Furthermore the limited number of species aforementioned above and disclosed in the specification is not deemed to be representative of the genus of GWT1 gene encompassed by the instant claims. Moreover, Applicant is reminded that adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. Therefore, although the specification discloses examples GWT1 gene, the specification does not teach any structural limitations and the specification is silent to the correlation of its recited function.

Moreover, the specification discloses proteins and protein mutants can be prepared by hybridization techniques normally have high homology to proteins consisting of the amino acid sequence (see pg. 3 lines 15-25). The specification does not describe any DNA variants generated from mutations: substitution, deletion, insertion, addition (e.g., fusion), any protein mutants encoded by the DNA variant thereof capable of decreasing of glycosaminyl-acylphosphatidylinositol (GlcN-(acyl)PI) and the capability of inhibiting fungal glycosylphosphatidylinositol (GPI) anchored protein in the cell wall of fungus. The specification does not describe any sequences and/or fragments which hybridize to any nucleotide as claimed capable of decreasing of GlcN-(acyl)PI and capable of inhibiting fungal GPI anchored protein in the cell wall of fungus.

The specification doesn't explicitly define what constitutes stringent conditions. Therefore a DNA hybridizing to the DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13 under stringent conditions leads to unpredictable results. Moreover, hybridization under stringent conditions would be expected to permit a great deal of variation between the two hybridizing sequences, making it even more unpredictable that the two sequences would share the same function.

Moreover, the scope of the claims includes numerous structural variants/analogues, and the genus is highly variant because a significant number of structural differences between genus members are permitted. Therefore the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant to screen for a compound having antifungal activity in the method as claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. As to the aforementioned method, the claims are drawn to a large number functional analogue of variants and a polypeptide coded by variants having different possibilities of changes to the amino acid sequences as claimed. The specification does not teach an example of any functional analogue of variants and a polypeptide coded by variants that comprise the method of screening for a compound having any antifungal activity.

Without structural limitations in the claimed method comprising , (a) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; (b) a DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13; (c) a DNA hybridizing to the DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13 under stringent conditions; (d) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; and (e) a DNA encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14, wherein one or more amino acids have been added, deleted, substituted, and/or inserted of the screening of a compound having antifungal activity in any method; the written description is not deemed to be fulfilled and the specification lacks proper written description of the claimed method as set forth *supra*. This issue is best resolved by Applicants pointing to the specification by page and line number where description of the claimed invention is set forth.

Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of (a) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; (b) a DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13; (c) a DNA hybridizing to the DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13 under stringent conditions; (d) a DNA encoding a protein comprising the amino acid sequence of SEQ

ID NO: 2, 4, 6, 8, 10, or 14, (e) a DNA encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14, wherein one or more amino acids have been added, deleted, substituted, and/or inserted, the screening of a compound having antifungal activity for the claimed method, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of GWT1 gene. Therefore, in accordance with the Guidelines, the description is not deemed representative and thus does not meet the written description requirement.

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Enablement

6. The rejection of claims 1-6 and 9-10 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for the reasons set forth in the previous office action. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a enablement rejection.

Applicants arguments filed in response to the 35 U.S.C. 112 first paragraph, February 8, 2010 is carefully considered, but not found to be persuasive for the reasons below.

Applicant argues:

A) As an initial matter, Applicants note that the Examiner has apparently misunderstood the function of GWT1. For example at page 6, lines 25-27 of the Office Action, the Examiners states that "[t]he specification is only limited the S. Cerevisiae GWTI gene comprising the nucleotide sequence of SEQ 1I) NO: 1 capable of decreasing GlcN-(acyl)PI" (emphasis added). In fact, as discussed above, the function of GWT1 is to catalyze the transacylation of GPI, thus forming GlcN-(acyl)PI. Activity of the enzyme therefore leads to increased levels of GlcN-(acyl)PI, not decreased levels. While not necessarily agreeing with the Examiner's assertions, the Applicants have amended claim 2 to further specify the claimed proteins. Specifically, stringent conditions have been defined in claim 2(c) and the number of amino acid residues which have

been added, deleted, substituted, and/or inserted has been specified in claim 2(d). Furthermore, a DNA has been added in claim 2(e), encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14. As explained in detail below, the DNAs of amended claim 2(c), (d) and (e) would be expected to encode proteins having the same function of the original GWT1 as set forth SEQ ID NOs: 2,4,6,8, 10, or 14 as explained below.

B) Applicants provide herewith two references published after filing date of the present application. The first reference, Umemura, et al (J. Biol. Chem. 278:23639-23647 (2003), Appendix A) teaches that GWT1 of Schizosaccharomyces pombe and Cryptococcus neoformans catalyze the transacylation of GPI (see page 23664, lines 16-23 of right column). In addition, pair-wise alignments between the amino acid sequences of GWT1 of Saccharomyces cerevisiae ("EI-A0209P-2", SEQ ID NO: 2), Schizosaccharomycespombe ("EI-A0209P-8", SEQ ID NO: 8) and Cryptococcus neoformans ("E1-A0209P-14", SEQ ID NO: 14) are shown in the attached Appendix B. These alignments show that the identity between these three amino acid sequences is at least about 30%. Thus, one of skill would recognize that a protein comprising an amino acid sequence having as little as about 30% identity to one of these three amino acid sequences would also catalyze the transacylation of GPI.

C) The second reference, Murakami, et al (Mol. Biol. Cell 14:4285-4295 (2003), Appendix C) teaches that a rat enzyme identified as PIG-W (GWT1) catalyzes the transacylation of GPI (see "PIG- WIs Most Likely the Acyltransferase" at page 4289, right column). In addition, alignment results between the amino acid sequences of GWT 1 of Saccharomyces cerevisiae and rat PIG- W (Genbank accession no. BAC77020) are shown in the attached Appendix D. The results indicate that the identity between these two amino acid sequences is also about 30%. This information provides further evidence to show that a protein comprising a amino acid sequence as little as about 30% identical to one of these two amino acid sequences catalyzes the transacylation of GPI.

D) The proteins encoded by the DNAs of amended claim 2(d) and (e) comprise a amino acid sequence having more than 60% identity to these three amino acid sequences, and thus it would be recognized that the claim is directed to proteins that catalyze the transacylation of GPI. Also, since stringent conditions have been defined in claim 2(c), DNAs encoding a protein having less than 30% identity to these three amino acid sequences would not be encompassed in

the DNA of amended claim 2(c). Moreover, the specification provides clear instructions and actual examples of methods for testing transacylation of GPI (see 2. Methods for determining transacylation activity, beginning on page 6 of the present application). Thus, variants can be readily tested for this activity. Accordingly, in view of the evidence provided here, one of skill would recognize that GWT1 variants as defined by amended claim 2 will catalyze transacylation of GPI and would thus be useful in the claimed methods.

E) The Examiner also questions whether there is a correlation between compounds identified by the claimed methods and antifungal activity. However, US 2004/0038239 (Appendix E) corresponding to US Application No. 10/332,340 discloses that compounds identified by the claimed methods (for example 1-(4-butylbenzyl) isoquinoline, which is described on pages 10-11 of the present application) have antifungal activity and inhibit the growth of Saccharomyces cerevisiae and Candida albicans. Thus, compounds identified by the claimed methods clearly correlate with the antifungal activity.

Examiners Response to Applicants Arguments:

With regard to Points (A), (B), and (D), the Examiner understands the function of GWT1 is to catalyze the transacylation of GPI, thus forming GlcN-(acyl)PI. Activity of the enzyme therefore leads to increased levels of GlcN-(acyl)PI, not decreased levels. Furthermore, a reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. The specification discloses only the detection of acylated GPI in GWT1 gene-introduced wild-type strain isolated from *Saccharomyces Cerevisiase (S. Cerevisiase).* The specification states the compounds of Examples (B2, B60, B73, and B85) disclose the GWT1 gene. The specification discloses that acylated GPI was inhibited by compounds in example B2 and B60 (see Figure 4). Therefore the specification only contemplates GWT1 gene can be screened using acylated GPI (GlcN-(acyl)PI) as an indicator because the compounds as set forth supra inhibit GlcN-(acyl)PI. Hence, the correlation between the detection of acylated GPI in said GWT1 gene-introduced wild-type strain merely suggest that GlcN-(acyl)PI decreased in a test sample having antifungal activity will indicate inhibitory activity of GWT1 gene in an assay (see pg. 10 lines 1-15). The specification is only limited the *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) comprising the nucleotide sequence of SEQ ID NO:1 capable of increasing GlcN-(acyl)PI and the detection of an acylated GPI in GWT1 gene-introduced wild-type strain isolated from

Saccharomyces Cerevisiase (S. Cerevisiase). Furthermore, Applicants have not shown how GlcN-(acyl)PI can be used as an indicator, when GlcN-(acyl)PI is added to a test sample with any overexpressed protein encoded by GWT1 gene resulting in GlcN-(acyl)PI decreased in the sample. In regards Applicants response of DNA hybridization in 2(c) aforementioned above, the specification doesn't explicitly define what constitutes stringent conditions. Therefore, the disclosure fails to describe common attribute and characteristics that identify the variant polynucleotides and/or the subsequences that hybridizing to the full-length SEQ ID NO: 1 sequence, which have the biological activity. In regards Applicant response that the proteins encoded by the DNAs of amended claim 2(d) and (e) comprise a amino acid sequence having more than 60% identity to these three amino acid sequences aforementioned above, screening and characterizing the variant sequences or fragments require undue experimentation because targeting polynucleotide variants, cloning, expressing, and characterizing the nucleotide sequences encoding functional (e.g., anti-fungal) proteins still require a large quantity of experimentation.

Consequently, Applicant has not shown the correlation of structure of *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) (or any fragment, complement etc.) in a test sample having antifungal activity capable of screening for antifungal activity in a test sample comprising method steps 1), 2), and 3) as claimed. Therefore, the performance of said method steps 1) 2) and 3) do not correlate to the outcome as claimed. In view of the quantity of experimentation necessary, the limited working examples and the breadth of the claims, it would take undue trials and errors to practice the claimed invention. Thus, the amount and level of experimentation needed is undue. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

With regard to Points (B) and (C), the Umemura, et al (J. Biol. Chem. 278:23639-23647 (2003), disclose mutations (substitutions): W63R and V64A of S. Cerevisiae Gwtl gene (see Figure 5) that result in a temperature sensitive (Ts) phenotype which cause the Gwt1 loss of function (see page 23642, the left column, the 1st paragraph, the last sentence). Furthermore, the pair-wise alignments between the amino acid sequences of GWT1 of Saccharomyces cerevisiae ("EI-A0209P-2", SEQ ID NO: 2), Schizosaccharomycespombe ("EI-A0209P-8", SEQ ID NO: 8) and Cryptococcus neoformans ("E1-A0209P-14", SEQ ID NO: 14) shown in the attached

Appendix B in Figure 5 only suggest that the mutations to the GWT1 gene can lead to a predictable outcome. Furthermore, the second reference, Murakami, et al (Mol. Biol. Cell 14:4285-4295 (2003), Appendix C) teaches that a rat enzyme identified as PIG-W is responsible for inositol acylation and only suggest the GWT1 gene responsible for catalyzing the transacylation of GPI is complementary.

The general knowledge and level of skill in the art do not supplement the omitted description with respect to a massive number of variant sequences of peptide. An unduly level of skill is needed for the skilled artisan in order to make and characterize the variant polynucleotides and the subsequences thereof. It is noted that applicant(s) have listed nucleotide sequences (GWT1 genes of yeast strains, e.g., S. cerevisiae, from 8 different species (SEQ ID) NOs l, 3, 5, 7, 9, 11-13) which are known in the prior art and which has a percentage similarity to a claimed sequence. Absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effect of these changes are largely unpredictable as to which one have significant effect versus not. Therefore, the references of Umemura, et al and Murakami, et al cited by Applicants in regards to sequence similarity results are unpredictable and therefore unreliable correspondence between the claimed method. The biomolecule and the indicated similar biomolecule of known function lack support regarding written description. Screening and characterizing the variant sequences or fragments require undue experimentation because targeting polynucleotide variants, cloning, expressing, and characterizing the nucleotide sequences encoding functional (e.g., anti-fungal) proteins still require a large quantity of experimentation. Therefore, Applicant's response that one of skill would recognize a protein comprising an amino acid sequence having as little as about 30% identity to one of these three amino acid sequences is unpersuasive and would not catalyze the transacylation of GPI.

With regard to Point (D), in regards to Applicant response that the proteins encoded by the DNAs of amended claim 2(d) and (e) comprise a amino acid sequence having more than 60% identity to these three amino acid sequences, absent factual evidence, a percentage sequence

similarity of less than 100% is not deemed to reasonably support to one skilled in the art whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effect of these changes are largely unpredictable as to which one have significant effect versus not. Thus the 2(d) and 2(e) aforementioned above are not representative of the genus of GWT1 gene for the recited function in the method as claimed and would not be recognized or directed to proteins that catalyze the transacylation of GPI.

The instant claim language with respect to the hybridization (resulting in a large number of the variant polynucleotides) would render the claims so broad that the scope of claims is outside the bounds of the enablement and would have resulted in the necessity of undue experimentation. Moreover, the specification discloses proteins and protein mutants can be prepared by hybridization techniques normally have high homology to proteins consisting of the amino acid sequence (see pg. 3 lines 15-25). The specification doesn't explicitly define what constitutes stringent conditions. The mere fact that two nucleic acid sequences will hybridize under moderate or stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus, correlation between the structure and function of the claimed invention does not meet the written description requirements. Further, it is well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability with respect to the full-length nucleic acid is possible, however the claims also read on nucleotide subsequences or fragment. Finally, hybridization under conditions even high stringency would be expected to permit a great deal of variation between the two hybridizing sequences, making it even more unpredictable that the two sequences would share the same function. Thus, the recitation of "a DNA that hybridizes under stringent condition to a DNA ..." actually reads onto "percent identity" language. Thus, as for the recitation of percent identity, hybridization language in the absence of a testable function and limitations regarding both the hybridization conditions and the sequence length over which the hybridization takes place, does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

With regard to Point (E), there is no correlation between the compounds and the method of screening for a sample as claimed. The US 2004/0038239 (Appendix E) corresponding to US Application No. 10/332,340 disclose the compound (for example 1-(4-butylbenzyl) isoquinoline. The specification only discloses said compound having inhibitory activity in GPI acylation (see pages 10-11 of the present application). However the data stated does not represent the claimed method for screening for antifungal activity in a test sample with GWT1 gene. Moreover, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the compound aforementioned above and identified by the claimed method that and inhibit the growth of Saccharomyces cerevisiae and Candida albicans) are not recited in the rejected claim(s).

As outlined previously, while being enabling for a method of detecting the function of GWT1 gene, wherein the method comprises the steps of: (1) contacting a test sample with an overexpressed protein (SEQ ID NO:2) encoded by the GWT1 gene (SEQ ID NO: 1); (2) detecting GlcN-(acyl)PI; and (3) selecting the test sample that decreases GlcN-(acyl)PI, does not reasonably provide enablement for a method of screening for a compound having an antifungal activity, wherein the method comprises the steps of: (1) contacting a test sample with an overexpressed protein encoded by the GWT1 gene; wherein the GWT1 gene is any one of the following: (a) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; (b) a DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13; (c) a DNA hybridizing to the DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13 under stringent conditions in 4x SCC at 65°C followed by washing with 0.1X SSC at 65°C for one hour; (d) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; and (e) a DNA encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14, wherein one or more amino acids have been added, deleted, substituted, and/or inserted (2) detecting GlcN-(acyl)PI; and (3) selecting the test sample that decreases GlcN-(acyl)PI. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).
There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:
(A) The breadth of the claims;
(B)The nature of the invention;
(C)The state of the prior art;
(D)The level of one of ordinary skill;
(E)The level of predictability in the art;
(F)The amount of direction provided by the inventor;
(G)The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention

The claims are drawn to a method of screening for a compound having an antifungal activity, wherein the method comprises the steps of: (1) contacting a test sample with an overexpressed protein (SEQ ID NO:2) encoded by the GWT1 gene (SEQ ID NO: 1); (2) detecting GlcN-(acyl)PI; and (3) selecting the test sample that decreases GlcN-(acyl)PI, does not reasonably provide enablement for a method of screening for a compound having an antifungal activity, wherein the method comprises the steps of: (1) contacting a test sample with an overexpressed protein encoded by the GWT1 gene; wherein the GWT1 gene is any one of the following: (a) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; (b) a DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13; (c) a DNA hybridizing to the DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13 under stringent conditions in 4x SCC at 65°C followed by washing with 0.1X SSC at 65°C for one hour; (d) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; and (e) a DNA encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or

14, wherein one or more amino acids have been added, deleted, substituted, and/or inserted (2) detecting GlcN-(acyl)PI; and (3) selecting the test sample that decreases GlcN-(acyl)PI.

The breadth of the claims

The product being used to screen for a compound having antifungal activity comprises:

(a) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14;

(b) a DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13;

(c) (c) a DNA hybridizing to the DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13 under stringent conditions in 4x SCC at 65°C followed by washing with 0.1X SSC at 65°C for one hour;

(d) a DNA encoding a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14; and

(e) a DNA encoding a protein which has more than 60% identity to the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, or 14, wherein one or more amino acids have been added, deleted, substituted, and/or inserted, wherein one or more amino acids have been added, deleted, substituted, and/or inserted is overly broad. Therefore it is hard for one skilled in the art to determine if steps 1) contacting a test sample with an overexpressed protein encoded by the GWT1 gene, 2) detecting GlcN-(acyl)PI; and 3) selecting the test sample that decreases GlcN-(acyl)PI can be used for screening for a compound having antifungal activity.

The Quantity of Experimentation Required

The quantity of experimentation required to practice the invention as claimed would be undue as it would require novel and unknown species that will correlate to steps 1) 2) and 3) as set forth *supra* to screen for a compound having antifungal activity. Since the specification fails to provide particular guidance for screen for a compound having antifungal activity as set forth supra it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Guidance in the specification/Working Examples

The specification discloses only the detection of acylated GPI in GWT1 gene-introduced wild-type strain isolated from *Saccharomyces Cerevisiase (S. Cerevisiase).* The specification states the compounds of Examples (B2, B60, B73, and B85) disclose the GWT1 gene. The specification discloses that acylated GPI was inhibited by compounds in example B2 and B60 (see Figure 4). Therefore the specification only contemplates GWT1 gene can be screened using acylated GPI (GlcN-(acyl)PI) as an indicator because the compounds as set forth supra inhibit GlcN-(acyl)PI. Hence, the correlation between the detection of acylated GPI in said GWT1 gene-introduced wild-type strain merely suggest that GlcN-(acyl)PI decreased in a test sample having antifungal activity will indicate inhibitory activity of GWT1 gene in an assay (see pg. 10 lines 1-15). Additionally, there is no correlation between the method steps and the preamble of screening a test sample having antifungal activity in the method as claimed. The specification is only limited the *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) comprising the nucleotide sequence of SEQ ID NO:1 capable of increasing GlcN-(acyl)PI and the detection of an acylated GPI in GWT1 gene-introduced wild-type strain isolated from *Saccharomyces Cerevisiase (S. Cerevisiase).* Furthermore, Applicants have not shown how GlcN-(acyl)PI can be used as an indicator, when GlcN-(acyl)PI is added to a test sample with any overexpressed protein encoded by GWT1 gene resulting in GlcN-(acyl)PI decreased in the sample. The specification doesn't define hybridization under stringent conditions. Therefore a DNA hybridizing to the DNA comprising the nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 12, or 13 under stringent conditions which leads to unpredictable results. Moreover, hybridization under stringent conditions would be expected to permit a great deal of variation between the two hybridizing sequences, making it even more unpredictable that the two sequences would share the same function. Moreover, the scope of the claims includes numerous structural variants/analogues, and the genus is highly variant because a significant number of structural differences between genus members are permitted. The disclosure fails to describe the common attributes or characteristics that identify members of the genus because the genus is highly variant in a sample in the method of screening a sample having antifungal activity. As to the aforementioned method, the claims are drawn to a large number functional analogue of variants and a polypeptide coded by variants having different possibilities of changes to the amino acid sequences as claimed.

The specification does not teach an example of any functional analogue of variants and a polypeptide coded by variants that comprise the method of screening for a compound having antifungal activity. Since the disclosure fails to provide any working example of steps 1), 2), and 3) correlating with the function as claimed nor has the disclosure shown variant polynucleotides and/or the subsequences that hybridize the genus to correlate with function as claimed, the specification as filed fails to provide guidance with the method of screening a compound as set forth supra. Consequently, Applicant has not shown the correlation of structure of *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) (or any fragment, complement etc.) in a test sample capable of screening for antifungal activity comprising method steps 1), 2), and 3) as claimed. Furthermore, Applicant has not shown the correlation of the genus of GWT1 gene (SEQ ID NOs: 1, 3, 5, 7, 9, 11-13), with the functional limitations aforementioned above.

In conclusion, the claimed inventions are not enabled for a method of screening for a compound having an antifungal activity, wherein the method comprises the steps of: (1), (2), and (3). The product comprising (a), (b), (c), (d), and (e) being used for screening the compound as set forth supra is overly broad. Therefore the specification only contemplates that compounds inhibiting GWT1 gene can be screened using acylated GPI as an indicator. The specification is only limited to overexpression of the *S. Cerevisiae* GWT1 gene (SEQ ID NO: 1) comprising the nucleotide of SEQ ID NO:1 increasing GlcN-(acyl)PI and the detection of an acylated GPI in GWT1 gene-introduced wild-type strain isolated from S*accharomyces Cerevisiase (S. Cerevisiase)*.The specification doesn't define hybridization under stringent conditions. Moreover, hybridization under stringent conditions would be expected to permit a great deal of variation between the two hybridizing sequences, making it even more unpredictable that the two sequences would share the same function. The specification does not teach an example of any functional analogue of variants and a polypeptide coded by variants that comprise the method of screening for a compound having antifungal activity. In view of the quantity of experimentation necessary, the limited working examples and the breadth of the claims, it would take undue trials and errors to practice the claimed invention. Thus, the amount and level of experimentation needed is undue. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Conclusion

7. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/
for Nina Archie, Examiner of Art Unit 1645